

REMARKS/ARGUMENTS

Claims 15-17 and 22-24 are active.

Support for the amendment to Claim 15 is found in Claim 19 (protein as FSH) and on page 11, line 15 and the Examples on pages 12-34.

No new matter is added.

Applicants thank the Examiner for the courtesy of meeting with their undersigned representative on March 24, 2009 to discuss the claims of this application and the cited art. The substance of this discussion is summarized and expanded upon in the remarks below.

The claims of this application are directed to a method for the chromatographic analysis of total FSH (follicle stimulating) protein in which a poloxamer surfactant is added to the protein solution during the analysis. According to the specification on pages 3 and 4 the addition of the poloxamer surfactant avoids protein loss and does not interfere with analysis in determining purity and concentration. The examples of this application provide a number of statistical analyses demonstrating that this is the case.

In the Action, the claims have been newly rejected based primarily on the publication of Katakam et al for Claims 15-17 and 22-23; with Wen for Claim 18, with Wu for Claim 19 with Arduini for Claims 20 and 21, and with Toschi for Claim 24.

According to the rejections, Katakam describes detecting the quantity of protein and that the inclusion of the calibration curve was known and therefore obvious. As a first point, there is no evidence cited in the rejection that supports the position that following what Katakam teaches one would use a calibration curve. Obviousness rejections must be based on objective evidence of record. Cf. In re Lee, 277 F.3d 1338, 1343, 61 USPQ2d 1430, 1433 (Fed. Cir. 2002) (“ ‘The factual inquiry whether to combine references must be thorough and searching.’ ...It must be based on objective evidence of record. This precedent has been

reinforced in myriad decisions, and cannot be dispensed with.”). For these reasons, it is requested that the rejections be withdrawn.

Second, Katakam is reporting on stability of HGH in various processing steps and more specifically the formation of aggregates (see the Abstract as an example). The Examiner cites to the 1<sup>st</sup> paragraph in col. 2 of page 145 as teaching quantifying the protein. However, Katakam is only assessing soluble vs. insoluble aggregates, and in particular the non-covalent nature of those aggregates, not the total quantity of the protein as defined in the claims presented here.

During the above-noted discussion, the Examiner’s pointed, for example, to the teachings on page 145, column 2, where Katakam describes analyzing the soluble aggregates which is asserted to be a quantity of the protein even if only a subset of the total protein. The Examiner maintained that Katakam describes the utility of using the surfactant for reducing aggregates. However, as is clear from Katakam, he is only assessing the aggregation effects not assessing the total protein content in the sample (Cf. amended Claim 15).

Further as conceded in the rejections, Katakam does not describe FSH only HGH (human growth hormone). Indeed, there are no teachings in Katakam that allow one to envision the effects of Poloxamer surfactants on FSH as claimed even in view of the largely omnibus and unsupported conclusion cited at page 3 of the Action in rejecting Claim 19 combining Wu with Katakam. While it is true that Wu describes isolating FSH from bovine pituitary glands and Katakam discusses effects of HGH aggregation in the presence of poloxamer, there are no teachings in this combination of art that even remotely suggests any problems with FSH.

HGH and FSH are very different proteins, have remarkably different structures and how one protein (HGH) acts in a given set of experiments (like in Katakam) provides no reasonable guidance as to how a second, distinct protein (FSH from Wu) would behave.

HGH is a protein of about 200 amino acids and a molecular weight of 22 KD. The structure includes four helices for functional interaction with its receptor. The three-dimensional structure of HGH reported at RCSB Protein Databank (<http://www.rcsb.org/pdb/home/home.do>) is:



In contrast, FSH is a glycoprotein composed of two polypeptide monomers,  $\alpha$  and  $\beta$ . The three-dimensional structure of FSH reported at RCSB Protein Databank (<http://www.rcsb.org/pdb/home/home.do>) is:



The combination of Katakam and Wu (or for that matter the other cited references of Wen, Arduini, and Toschi) do not provide any teachings as to how to assess total FSH protein in a chromatographic method as is defined in the claims.

Persons having ordinary skill in the art normally seek "to improve upon what is already generally known." *In re Peterson*, 315 F.3d 1325, 1330 (Fed. Cir. 2003). However,

before persons having ordinary skill in the art would want to optimize the choice or use of components in a claimed process, the prior art must at least generally recognize the process and generally suggest the components the claimed process utilizes to achieve its goals. To establish that Applicants' claimed process would have been obvious to a person having ordinary skill in the art, the prior art must reasonably suggest that persons having ordinary skill in the art do what Applicants claims require. Here, the only suggestion to do what Applicants have done is Applicants' own disclosure, i.e. hindsight.

Where, as here, the rejection of the subject matter Applicants claim is based on hindsight, the rejection is improper. *In re Fritch*, 972 F.2d at 1266; *In re Fine*, 837 F.2d at 1075.

Reconsideration and Withdrawal of the rejection is requested.

Allowance of this case is requested.

Respectfully submitted,

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